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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/062,587	01/31/2002	Harvey D. Preisler	047940-0135	1948

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/062,587	PREISLER, HARVEY D.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *22-31,34-38 and 46-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,3-17,21 and 39-45* is/are rejected.

7)☐ Claim(s) *2,18-20,32 and 33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/11/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicants election with traverse of Group I, drawn to peptides and the election of the species of SEQ ID NO:7. The traversal is on the grounds that it would not be undue burden to search both the product and the method claims together. This has been considered but not found persuasive. As stated in the previous Office action, the separation of product and method claims is proper if the product can be demonstrated to be independent of the claimed method of use. Further, the groups are classified differently requiring different searches in the U.S. patent shoes, and consideration of different issues of patentability. Thus, the search and the examination of both groups would not be co-extensive and constitute an undue search burden on the examiner. For these reasons the restriction requirement is deemed proper and adhered to. The restriction is thus made FINAL. With regard to the species election and applicants request that more than one species be examined, all the claimed peptides were examined. It was noted that polypeptides comprising the elected SEQ ID NO:7 as well as polypeptides comprising SEQ IDNO:1-23 and 26-31 are free of the art; polypeptides comprising one or more conservative amino acid substitutions were not free of the art, however, in the interest of advancing prosecution, Group I was examined to the full scope of the claims. Please note that the search for the polypeptides of SEQ ID NO:1-23 and 26-31 and conservative variants thereof required some 363 separate steps on the databases available to the examiner and above that which was required for the broader search of claims 39-45 which was not limited by sequence identifiers.

Claims 1-51 are pending. Claims 22-31, 34-38 and 46-51, drawn to non-elected invetions, are withdrawn from consideration. Claims 1-21, 32, 33, 39-45 are examined on the merits.

Priority

Acknowledgement is made to applicant's claim to an earlier effective filing date via provisional application 60/278,465. Upon review of the '465 application it is noted that only SEQ ID NO:1-6 are disclosed, and that the induction of differentiation of leukemia cells and the subsequent inhibition of proliferation of said leukemia cells is not described in the '465 application. Thus,

the '465 application lacks adequate written description of the instant claimed invention. Accordingly the instant claims are given the effective filing date of January 31, 2002 .

Claim Objections

Claims 32 and 33 are objected to for being dependent on a nonelected claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-17, 21 and 39-45 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear how claims 3-17 further limit claim 1. Claim 1 recites "an isolated polypeptide comprising a sequence selected from sections A, B, C and D. The dependent claims 3-17 recites wherein the sequence is selected from SEQ ID NO:X and SEQ ID NO:Y; or in the case of claim 8, SEQ ID NO:8. It is unclear if the dependent claims include SEQ ID NO:X and SEQ ID NO:Y having one or more conservative amino acid substitutions, or if the dependent claims are limited to the sequences comprising SEQ ID NO:X or SEQ ID NO:Y. for purpose of examination, both alternatives will be considered.

Claim 21 recites "consisting essentially of". It is unclear how "consisting essentially of" differs from comprising.

Claim 39 is vague and indefinite in the recitation of "immunogenic molecule". The metes and bound of "immunogenic molecule" cannot be determined without reference to the host experiencing the immunogenicity. Any molecule can be immunogenic given an appropriate host which will recognize said molecule as a non-self molecule. For purpose of examination, the claim will be read with the proviso that the peptide does not bind to a cancer-associated antigen on the surface of the blood cell.

The recitation of "accessory molecule" in claim 43 lacks antecedent basis in claim 39. for purpose of examination claim 43 will be read as dependent on claim 42.

Claim 43 is unclear because the difference between a "tag molecule" and an "identification molecule" cannot be discerned.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 21 and 39-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn in part to an isolated polypeptide comprising a sequence selected from SEQ ID NO:1-23 or 26-31 having one or more conservative amino acid substitutions. Claim 21 embodies the isolated polypeptide of claim 1 wherein the polypeptide consists of, rather than comprises, SEQ ID NO:1-23 or 26-31 having one or more conservative amino acid substitutions. The claims encompass a genus of proteins which need not comprise any of the contiguous amino acids of SEQ ID NO:1-23 or 26-31 as conservative amino acid substitution of all the amino acids of SEQ ID NO:1-23 or 26-31 would be permitted in the genus. Further, the genus is not limited by functional attributes of the individual species. Thus, the genus is highly variant encompassing proteins and peptides which have not amino acid sequence similarity to the described SEQ ID NO:1-23 or 26-31 and which have functional characteristic which differ from those of SEQ ID NO:1-23 or 26-31 as evidenced by the art rejections below. In light of the prior art, it is clear that the written description of SEQ ID NO:1-23 or 26-31 does not adequately describe the claimed variant genus. One of skill in the art would reasonable conclude that applicant was not in possession of the claimed genus.

Claims 39-45 encompass a genus of protein which bind preferentially to a surface of a blood cell with the provision that the peptide does not bind to a cancer antigen on the surface of the blood cell. The claim encompasses peptides that bind to any protein which is not a tumor antigen on any type of blood cell. the genus would include peptide which bind to any cell surface structure such as a carbohydrate or the extracellular domain of any receptor, such as the MHC class I and II proteins, or receptors for transferring or folate on any blood cell which includes platelets, monocytes, T-cells, B-cells, erythrocytes. thus, the genus of peptides is highly variant encompassing proteins which do not have common structural or functional attributes. The disclosure of SEQ ID NO:1-23 and 26-41 does not adequately describe the claimed genus, because these peptides do not exhibit a representative number of structural and functional characteristics comprised within the claimed genus.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 39, 40, 44 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by the abstract of Nakaya et al (Biochemistry International, 1985, Vol. 10, pp. 619-626) or the abstract of Ajinomoto (EP 210,461).

Claim 39 is drawn to an isolated polypeptide comprising a binding region which binds preferentially to a surface of a blood cell with the provision that the peptide does not bind to a cancer associated antigen on the surface of the blood cell. Claim 40 embodies the peptide of claim 39 wherein the blood cell is a leukemia cell. Claim 44 embodies the method of claim 39 wherein the polypeptide indices differentiation of the leukemia cell into a mature blood cell capable of normal blood cell function. Claim 45 embodies the peptide of claim 40 wherein the polypeptide inhibits the proliferation of the leukemia cell.

The abstract of Nakaya et al (Biochemistry International, 1985, Vol. 10, pp. 619-626) discloses the differentiation factor for mouse myeloid leukemia cells.

The abstract of Ajinomoto (EP 210,461) discloses a BUF-3 polypeptide capable of differentiating and maturing human leukemia cells into normal cells.

Claims 39, 40 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by the abstract of Steube et al (Leukemia, 1992, vol. 6, pp. 1048-1053).

The specific limitations of the claims are set forth above.

The abstract of Steube et al (Leukemia, 1992, vol. 6, pp. 1048-1053) discloses dolastatin 10 and dolastatin 15 which inhibited the growth of peripheral blood cells taken from patients with acute myeloid leukemia

Claims 39, 40, 41, 45are rejected under 35 U.S.C. 102(b) as being anticipated by Vidovic and Toral (Cancer Letter, 1998, Vol. 128, pp. 127-135).

The specific limitations of claims 39, 40 and 45 are set forth above. Claim 42 embodies the polypeptide of claim 39 wherein the polypeptide comprises a part of a carrier protein.

Vidovic and Toral (Cancer Letter, 1998, Vol. 128, pp. 127-135) disclose a monoclonal antibody which binds to HLA-DR of tumor B-cells and induces selective apoptosis in malignant B-cells (abstract, and page 130, second column, first and second full paragraphs). It s noted that the HLA-DR is not a cancer associated antigen, and would not be expected to be immunogenic in the subject in which the malignant B cells originated or a syngenic individual. The HLA-DR antibody comprising a peptide binding region to the HLA-DR molecule on the surface of a B-cell and an Fc region. the Fc regions inherently fulfills the specific embodiment of claim 42 drawn to a carrier protein. It is well known in the art that the Fc region increases the half-life of a protein in the blood; thus, the Fc region of the HLA-DR antibody metes the limitation of a carrier protein.

Claims 1, 4 and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Database Caplus on STN, Accession Number 2001:624615, Shimkets et al (WO 01/47944) discloses a

protein sequence comprising a conservative variant of SEQ ID NO:2 as indicated by the underlined area.

Claims 1, 3 and 21 Claims are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 2000:384488, Pelletier et al (WO 00/32835) disclose a protein sequence comprising a conservative variant of SEQ ID NO:1 as indicated by the underlined area.

Claims 1, 5 and 21are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 2000:384548, Ruvkun et al (WO 00/33068) discloses a protein sequence comprising a conservative variant of SEQ ID NO:3 as indicated by the underlined area.

Claims 1, 7 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 2000:260339, Panayi et al (WO 00/21995) discloses a protein sequence comprising a conservative variant of SEQ ID NO:4 as indicated by the underlined area.

Claims 1, 8 and 21are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1995:471011, Coombs et al (Bioorganic and Medicinal Chemistry Letters, 1995, Vol. 5 pp. 611-614) discloses a protein sequence comprising a conservative variant of SEQ ID NO:5 as indicated by the underlined area.

Claims 1, 9 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1999:691218, Arigoni et al (WO 99/54473) discloses a protein sequence comprising a conservative variant of SEQ ID NO:6 as indicated by the underlined area.

Claims 1, 7 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 2000:9190, Mayer et al (Nature 1999, Vol. 402, pp. 769-

777) discloses a protein sequence comprising a conservative variant of SEQ ID NO:13 as indicated by the underlined area.

Claims 1, 11 and 21are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 2000:688390, Iggoet al (WO 00/56909) discloses a protein sequence comprising a conservative variant of SEQ ID NO:15 as indicated by the underlined area.

Claims 1, 12 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1995:28511, Parker et al (Gene, 1994, Vol. 145, pp. 135-138) discloses a protein sequence comprising a conservative variant of SEQ ID NO:16 as indicated by the underlined area.

Claims 1, 13 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1999:9856, Madura (WO 98/57978) discloses a protein sequence comprising a conservative variant of SEQ ID NO:19 as indicated by the underlined area.

Claims 1, 10 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 2000:227762, Acton et al (WO 00/18899) discloses a protein sequence comprising a conservative variant of SEQ ID NO:21 as indicated by the underlined area.

Claims 1, 14 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1999:126776, Schatz (US 5,874,239) discloses a protein sequence comprising a conservative variant of SEQ ID NO:22 as indicated by the underlined area.

Claims 1, 15 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1998:267798, Wang et al (FEBS Letters, 1998, Vol. 427,

pp. 103-108) discloses a protein sequence comprising a conservative variant of SEQ ID NO:27 as indicated by the underlined area.

Claims 1, 16 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1998:26477, Hanada et al (Journal of Biological Chemistry, 1997, Vol. 272, pp. 32108-32114) discloses a protein sequence comprising a conservative variant of SEQ ID NO:28 as indicated by the underlined area.

Claims 1, 16 and 21are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1999:60870, Jacobs et al (Clinical and Diagnostic Laboratory Immunology, 1999, Vol. 6, pp. 24-29) discloses a protein sequence comprising a conservative variant of SEQ ID NO:29 as indicated by the underlined area.

Claims 1, 17 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Database Caplus on STN, Accession Number 1999:66315, Kool et al (Cancer Research, 1999, Vol. 59, pp. 175-182) discloses a protein sequence comprising a conservative variant of SEQ ID NO:30 as indicated by the underlined area.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 39, 40, 42, 43 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over the abstract of Steube et al (Leukemia, 1992, vol. 6, pp. 1048-1053).

The abstract of Steube et al (Leukemia, 1992, vol. 6, pp. 1048-1053) teaches dolastatin 10 and dolastatin 15 which inhibited the growth of peripheral blood cells taken from patients

with acute myeloid leukemia. the abstract further suggests that dolastatins in combination with other drugs could exert a role in the treatment of human myeloid leukemia. The abstract does not specifically teach dolastatins 10 and 15 further comprising a chemotherapeutic agent.

It would have been prima facie obvious at the time the invention was made to link dolastatins 10 and 15 to a chemotherapeutic agent active against leukemia. One of skill in the art would have been motivated to do so by the suggestion in the abstract of Steube to combine the dolastatins 10 and 15 with other drugs for the treatment of human myeloid leukemia.

KAC 5/3/2004

Claims 2 and 18-20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571)272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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